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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/917,376	07/28/2001	Shi-You Ding	NREL 01-36	9956

30955 7590 11/08/2005

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ART UNIT	**PAPER NUMBER**
1656	

DATE MAILED: 11/08/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/917,376	DING ET AL.	
	Examiner	Art Unit	
	Sheridan L. Swope	1656	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *September 2 & 29, 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,2,4-12,14,15,28,30-36,43 and 47-54* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,2,4-12,14,15,28,30-36,43 and 47-54* is/are rejected.

7)☒ Claim(s) *47,50,53 and 54* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

The Art Unit location of your application in the USPTO has changed. To aid in correlating any papers for this application, all further correspondence regarding this application should be directed to Art Unit 1656.

Applicant's Request for Continuing Examination and the amendment of September 2, 2005, in response to the Final Rejection of May 18, 2005, are acknowledged. Applicants were telephonically contacted by the Examiner on September 23, 27, and 28, 2005, requesting that a new copy of the claim set of September 2, 2005 be filed in order to correct improper formatting of Claims 47 and 50. It is acknowledged that a corrected claim set was filed as an amendment on September 29, 2005. It is acknowledged that Applicants have amended Claim 1 and added Claims 47-54. Claims 1, 2, 4-12, 14, 15, 28, 30-36, 43, and 47-54 are pending and are hereby considered.

Specification-Objections

Objection to the specification, for the multiple reasons listed in the Final Rejection of May 18, 2005 on pages 2-4, is maintained. In support of their request that said rejection be withdrawn, Applicants state that amendment to overcome said objections is made by way of a substitute specification filed September 2, 2005. However, the Office did not receive a substitute specification in Applicants' response of September 2, 2005 or September 29, 2005. Therefore, objection to the specification for the multiple reasons listed in the Final Rejection of May 18, 2005 is maintained.

The specification is objected to for containing hyperlinks, for example on page 23. USPTO policy does not permit the USPTO, i.e, via an issued patent, to link to any commercial

sites, since the USPTO exercises no control over the organization, views or accuracy of the information contained on these outside sites. Hyperlinks and other forms of browser-executable code, especially commercial site URLs, are not to be included in a patent application. (MPEP 608.01) The specification should be carefully checked and all URLs removed.

Claims-Objections

Claims 47, 50, 53, and 54 are objected to for the phrase "said catalytic domain GH74_Ace", which should be "said catalytic domain of GH74_Ace".

Claim Rejections - 35 USC § 112-Second Paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Rejection of Claims 1, 2, 4-11, 14, and 15 under 35 U.S.C. 112, second paragraph, for the reasons set forth in the Final Rejection of May 18, 2005 and the Action on the Merits of June 16, 2004, because the phrase "AviIII peptide" renders the claims indefinite is maintained. Claims 12 and 47-54 are herein rejected under 35 U.S.C. 112, second paragraph, for the same reasons.

In support of their request that said rejection be withdrawn, Applicants provide the following arguments. Claims 1, 2, 4-11, 14, and 15 define the recited polypeptide has having a certain degree of identity to SEQ ID NO: 1. It is unclear what better types of limitation the Examiner has in mind that would provide a better definition of the claimed composition. Retention of functionality is on the basis of 90% sequence identity.

These arguments are not found to be persuasive for the following reasons. It is acknowledged that Claim 1 has been amended to provide the structural limitation of at least 90% identity to SEQ ID NO: 1 and the functional limitation of cellulase activity. It is also

acknowledged that a polypeptide having at least 90% identity to SEQ ID NO: 1 and the functional limitation of cellulase activity is definitive. However, Claims 1, 2, 4-12, 14, 15, and 47-54 comprise the additional limitation of an "AviIII peptide", which as stated in the prior action, renders the claims indefinite. The specification fails to provide a concise definition of the term "AviIII peptide". The definition of an AviIII peptide, as provided on page 18 of the specification, states:

> "AviIII polypeptides of the invention include isolated polypeptides having an amino acid sequence as shown below in Example 1; Table 1 and in SEQID NO: 1, as well as variants and derivatives, including variants, having substantial identity to the amino acid sequence of SEQ ID NO:1 and that retain any of the functional activities of AviIII. AviIII polypeptide activity can be determined, for example, by subjecting the variant, derivative, or fragment to a substrate binding assay or a cellulase activity."

Said definition fails to provide any structural or functional limitations or definitions of the polypeptides encompassed. Therefore, although a polypeptide having at least 90% identity to SEQ ID NO: 1 and having cellulase activity is defined, said polypeptide having the additional limitation of being an AviIII peptide is indefinite. A person of ordinary skill in the art would not know the meets and bound of the recited invention. For these reasons and those set forth in the Final Rejection of May 18, 2005 and the Action on the Merits of June 16, 2004, rejection of Claims 1, 2, 4-12, 14, 15, and 47-54 are rejected under 35 U.S.C. 112, second paragraph, for being indefinite.

Rejection of Claims 1, 2, 4-11, 14, and 15 under 35 U.S.C. 112, second paragraph, for the reasons set forth in the Final Rejection of May 18, 2005, because the phrases "a catalytic domain of a glycosyl hydrolase family 74 (GH74_Ace) enzyme" and "carbohydrate binding domain (CBD)III" render the claims indefinite is maintained. Claims 47-54 are herein rejected under 35 U.S.C. 112, second paragraph, for the same reasons. In support of their request that said

rejection be withdrawn, Applicants state that that amendment of the specification to overcome said rejections is made by way of a substitute specification filed September 2, 2005. However, the Office has not received said substitute specification. Therefore, rejection of Claims 1, 2, 4-11, 14, and 15 under 35 U.S.C. 112, second paragraph, is maintained, while Claims 47-54 are herein rejected under 35 U.S.C. 112, second paragraph, for the same reasons. Applicant is reminded that any amendment to the specification that introduces New Matter cannot be entered.

Rejection of Claim 31 (rejected as Claim 32 in the prior action) under 35 U.S.C. 112, second paragraph, for the reasons set forth in the Final Rejection of May 18, 2005, because the phrase "substrate targeting moiety" renders the claims indefinite is maintained. In support of their request that said rejection be withdrawn, Applicants state that that amendment of the specification to overcome said rejection is made by way of a substitute specification filed September 2, 2005. However, the Office has not received said substitute specification. Therefore, rejection of Claim 31 under 35 U.S.C. 112, second paragraph, is maintained. Again, Applicant is reminded that any amendment to the specification that introduces New Matter cannot be entered.

Claims 1, 2, 4-12, and 47-54 are additionally rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention for the following reasons.

For Claims 1, 2, 4-12, and 47-54 the phrase "substantially purified" renders the claims indefinite because "substantially" is a relative term, which is not defined by either the specification or the claims. A person of ordinary skill in the art would not know the metes and bounds of the recited invention.

For Claim 6, the phrase "a polypeptide sequence identical to SEQ ID NO: 3" renders the claim indefinite. It is unclear whether the claim is meant to recite "the" polypeptide of SEQ ID NO: 3 or "any" polypeptide of SEQ ID NO: 3. The latter would encompass peptides as small as two residues. Clarification is required. For purposes of examination, it is assumed that Claim 6 is meant to recite the polypeptide sequence of SEQ ID NO: 3.

For Claim 12, the phrase "a polypeptide sequence of SEQ ID NO: 1" renders the claim indefinite. It is unclear whether the claim is meant to recite "the" polypeptide of SEQ ID NO: 1 or "any" polypeptide of SEQ ID NO: 1. The latter would encompass peptides as small as two residues. Clarification is required. For purposes of examination, it is assumed that Claim 12 is meant to recite the polypeptide sequence of SEQ ID NO: 1.

Claim Rejections - 35 USC § 112-First Paragraph

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Enablement

In this regard, the application disclosure and claims are compared per the factors indicated in the decision In re Wands 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988). These factors are considered when determining whether there is sufficient evidence to support a description that a disclosure does not satisfy the enablement requirement and whether any necessary experimentation is undue. The factors include but are not limited to: (1) the nature of the invention; (2) the breath of the claims; (3) the predictability or unpredictability of the art; (4) the amount of direction or guidance presented; (5) the presence or absence of working examples;

(6) the quantity of experimentation necessary; (7) the relative skill of those skilled in the art. Each factor is here addressed on the basis of a comparison of the disclosure, the claims, and the state of the prior art in the assessment of undue experimentation.

Rejection of Claims 1, 2, 4-11, 14, 15, 28, 30-36, and 43 under 35 U.S.C. 112, first paragraph, for lack of enablement, as set forth in the prior actions, is maintained. New Claim 53 is herein also rejected under 35 U.S.C. 112, first paragraph, for lack of enablement. Based on the instant amendment, the reasons for the rejection of Claims 1, 2, 4-11, 14, 15, 28, 30-36, 43, and 53 are as follows. While the specification is enabling for the polypeptide of SEQ ID NO: 1, it does not reasonably provide enablement for any cellulase having at least 90% identity to SEQ ID NO: 1 or any polypeptide having at least 90% identity to SEQ ID NO: 3 or comprising one or more of SEQ ID NO: 1, 3, 4, or 5. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Claims 1, 2, and 4-9, 14, and 15 are so broad as to encompass any polypeptide having at least 90% identity with SEQ ID NO: 1 and having cellulase activity. Claim 10 is so broad as to encompass any polypeptide having at least 90% identity with SEQ ID NO: 1, at least 90% identity to SEQ ID NO: 3, and having cellulase activity. Claim 11 is so broad as to encompass any polypeptide having at least 90% identity with SEQ ID NO: 1, at least 80% identity to SEQ ID NO: 3, and having cellulase activity. Claims 28, 30-36, and 43 are so broad as to encompass any polypeptide comprising one or more of SEQ ID NO: 1, 3, 4, or 5 and having any activity. Claim 53 is so broad as to encompass any polypeptide having at least 90% identity with SEQ ID NO: 3 and having any activity. The scope of each of these claims is not commensurate with the

enablement provided by the disclosure with regard to the extremely large number of polypeptides broadly encompassed by the claim. Since the amino acid sequence of a protein determines its structural and functional properties, predictability of which changes can be tolerated in a protein's amino acid sequence and obtain the desired activity requires a knowledge of and guidance with regard to which amino acids in the protein's sequence, if any, are tolerant of modification and which are conserved (i.e. expectedly intolerant to modification), and detailed knowledge of the ways in which the protein's structure relates to its function. However, in this case the disclosure is limited to the amino acid sequence of SEQ ID NO: 1.

While recombinant and mutagenesis techniques are known, it is not routine in the art to screen for multiple substitutions or multiple modifications, as encompassed by the instant claims. Furthermore, the positions within a protein's sequence where amino acid modifications can be made with a reasonable expectation of success in obtaining the desired activity/utility are limited in any protein and the results of such modifications are unpredictable (Galye et al, 1993; Whisstock et al, 2003). In addition, one skilled in the art would expect any tolerance to modification for a given protein to diminish with each further and additional modification, e.g. multiple substitutions.

The specification does not support the broad scope of Claims 1, 2, and 4-9, 14, and 15, which encompasses any polypeptide having at least 90% identity with SEQ ID NO: 1 and having cellulase activity. The specification does not support the broad scope of Claim 10, which encompasses any polypeptide having at least 90% identity with SEQ ID NO: 1, at least 90% identity to SEQ ID NO: 3, and having cellulase activity. The specification does not support the broad scope of Claims 11, which encompasses any polypeptide having at least 90% identity with

SEQ ID NO: 1, at least 80% identity to SEQ ID NO: 3, and having cellulase activity. The specification does not support the broad scope of Claims 28, 30-36, and 43, which encompasses any polypeptide comprising one or more of SEQ ID NO: 1, 3, 4, or 5 and having any activity. The specification does not support the broad scope of Claim 53, which encompasses any polypeptide having at least 90% identity with SEQ ID NO: 3 and having any activity. The specification does not support the broad scope of Claims 1, 2, 4-11, 14, and 15, 28, 30-36, 43, and 53 because the specification does not establish: (A) regions of the protein structure which may be modified without effecting the cellulase activity; (B) the general tolerance of the cellulase activity to modification and extent of such tolerance; (C) the activity of any polypeptide comprising one or more of SEQ ID NO: 1, 3, 4, or 5 or having at least 90% identity to SEQ ID NO: 3; (D) regions of the protein structure of any polypeptide comprising one or more of SEQ ID NO: 1, 3, 4, or 5 or having at least 90% identity to SEQ ID NO: 3 which may be modified without effecting the desired activity; (E) the general tolerance of the desired activity to modification of any polypeptide comprising one or more of SEQ ID NO: 1, 3, 4, or 5, and extent of such tolerance; (E) a rational and predictable scheme for modifying any residues with an expectation of obtaining the desired biological function; and (F) the specification provides insufficient guidance as to which of the essentially infinite possible choices is likely to be successful.

Thus, applicants have not provided sufficient guidance to enable one of ordinary skill in the art to make and use the claimed invention in a manner reasonably correlated with the scope of the claims broadly including any number of cellulases with an enormous number of amino acid modifications of the cellulase of SEQ ID NO: 1. In addition, applicants have not provided

sufficient guidance to enable one of ordinary skill in the art to make and use the claimed invention in a manner reasonably correlated with the scope of the claims broadly including any number of polypeptides comprising one or more of SEQ ID NO: 1, 3, 4, or 5 or having at least 90% identity to SEQ ID NO: 3. The scope of the claims must bear a reasonable correlation with the scope of enablement (In re Fisher, 166 USPQ 19 24 (CCPA 1970)). Without sufficient guidance, determination of the identity of sequences having the desired biological characteristics is unpredictable and the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue. See In re Wands 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988).

In support of their request that said rejection be withdrawn, Applicants provide the following arguments.

(A) Regarding the conservation of specific residues, as recited in prior Claim 1 and now recited in new Claims 47 and 50, said conserved residues are taught by Table 5 and Example 2 of the specification.

(B) Guo et al is exploring protein tolerance to random substitutions. The instant specification teaches the importance of conserving some amino acids, as evidence by sequence similarity between AviIII of Acidothermus and Avicelase III of Aspergillus. The functional limitations of thermal tolerability and cellulase activity are also recited.

These arguments are found to be persuasive or not persuasive for the following reasons.

(A) Reply: Regarding Claims 47, 48, 50, 51, and 54, this argument is found to be persuasive and said claims are not rejected under 35 U.S.C. 112, first paragraph, for lack of enablement.

(B) Reply: This argument is not found to be persuasive. It is acknowledged that Table 5 and Example 2 of the specification teach an alignment of AviIII of Acidothermus and Avicelase III of Aspergillus, wherein the conserved residues are indicated. However, 1, 2, 4-11, 14, 15, 28, 30-36, and 43 do not recite the limitation of said conserved residues being comprised within the recited polypeptides. Said claims recite any polypeptide having the structural limitation of at least 90% identity to SEQ ID NO: 1, wherein the substitutions are random. The calculations presented in the prior action, which are based on Guo et al, are relevant to said claims because, as acknowledged by Applicants, Guo et al explores protein tolerance to random substitutions.

Therefore, rejection of Claims 1, 2, 4-11, 14, 15, 28, 30-36, and 43 under 35 U.S.C. 112, first paragraph, for lack of enablement, is maintained, while new Claim 53 is herein rejected under 35 U.S.C. 112, first paragraph, for lack of enablement.

Written Description

Rejection of Claims 10 and 11 under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement, as described in the Action on the Merits of June 16, 2004 and the Final Rejection of May 18, 2005, is maintained. As previously explained, Claim 10 introduces the limitation of an AviIII "...wherein, the catalytic domain of GH74_Ace has at least 90% sequence identity with SEQ ID NO: 3", while Claim 11 introduces the limitation of an AviIII "...wherein, the catalytic domain of GH74_Ace has at least 80% sequence identity with SEQ ID NO: 3". Said limitations are not disclosed in the original specification or claims. Thus, rejection of Claims 10 and 11 under 35 U.S.C. 112, first paragraph, for introducing New Matter, is maintained.

In support of their request that said rejection be withdrawn, Applicants provide the following arguments. The specification provides "[t]he amino acid sequence of AviIII polypeptides of the invention is preferably at least about 60% identical, more preferably at least about 70% identical, or in some embodiments at least about 90% identical, to the Avilll amino acid sequence shown above in Table 3 and SEQ ID NO:1." (specification; page 20, last paragraph). Although SEQ ID NO: 3 is not mentioned in this sentence, Table 1 shows that SEQ ID NO: 3 is a part of SEQ ID NO: 1. One skilled in the art would appreciate that SEQ ID NO: 1 encompasses SEQ ID NO: 3 and that sequences that share identity to SEQ ID NO:1 would similarly share sequence identity to SEQ ID NO: 3.

These arguments are not found to be persuasive for the following reasons. It is noted that the above quote is from page 19, paragraph 1, not page 20, last paragraph. It is acknowledged that the specification discloses polypeptides having at least about 60%, 70%, or 90% identity to SEQ ID NO: 1 and that SEQ ID NO: 3 is contained within SEQ ID NO: 1. However, said disclosure does not describe the genus of any polypeptide having the limitation of having at least 90% identity to SEQ ID NO: 1 and having 90% identity to SEQ ID NO: 3. Likewise, said disclosure does not describe the genus of any polypeptide having the limitation of having at least 90% identity to SEQ ID NO: 1 and having 90% identity to SEQ ID NO: 3. Furthermore, the specification fails to describe or teach the structure of any representative species of said genera of polypeptides. Therefore, rejection of Claims 10 and 11 under 35 U.S.C. 112, first paragraph, for introducing New Matter, is maintained.

Rejection of Claims 28, 30-36, and 43 under 35 U.S.C. 112, first paragraph, for insufficient Written Description, because the specification does not contain a disclosure of the

function of all polypeptides comprising one or more of SEQ ID NO: 1, 3, 4, and 5 is maintained. The instant rejection was previously explained in the Action on the Merits of June 16, 2004 and the Final Rejection of May 18, 2005. Applicants did not response to this rejection.

Claims 47, 48, 50, 51, and 54 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claims contains subject matter that was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the Inventors, at the time the application was filed, had possession of the claimed invention. Claims 47, 48, 50, 51, and 54 introduce the limitation of an AviIII "...having a sequence identical to SEQ ID NO: 3 in each conserved position marked by an asterisk (*), as shown in the comparison to *Aspergillus aculeatus* Avicelase III(AviIII_Aace):". The original specification and claims fail to disclose said limitation of "identical to SEQ ID NO: 3 in each conserved position marked by an asterisk (*), as shown in the comparison to *Aspergillus aculeatus* Avicelase III(AviIII_Aace):". Thus, Claims 47, 48, 50, 51, and 54 are rejected under 35 U.S.C. 112, first paragraph, for introducing New Matter.

The instant rejection is identical to the prior rejection of Claims 1, 2, 4, 5, 7-11, 14, and 15 under 35 U.S.C. 112, first paragraph, for introducing New Matter, as set forth in the Final Rejection of May 18, 2005. In support of their request that said rejection be withdrawn, Applicants provide the following arguments, which are relevant to the instant rejection of Claims 47, 48, 50, 51, and 54. The conservation of specific residues is taught in the specification by Table 5 and Example 2. The sequence used for the alignment in Table 5 is SEQ ID NO: 3.

These arguments are not found to be persuasive for the following reasons. Again, it is acknowledged that Table 5 and Example 2 of the specification teach an alignment of AviIII of

Acidothermus and Avicelase III of Aspergillus, wherein the conserved residues are indicated. However, said teaching does not describe the genus of polypeptides having at least 90% or 99% identity to SEQ ID NO: 1 and having conservation of the specific residues disclosed by Table 5 as being conserved between AviIII of Acidothermus and Avicelase III of Aspergillus. The specification fails to describe or teach the structure of any representative species of said genera of polypeptides. For these reasons and those presented above, Claims 47, 48, 50, 51, and 54 are rejected under 35 U.S.C. 112, first paragraph, for introducing New Matter.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Rejection of Claims 1, 2, 4-12, 14, 28, 36, and 43 under 35 U.S.C. 102(b) as being anticipated by Adney et al, 1994 or Tucker et al, 1989, for the reasons set forth in the Final Rejection of May 18, 2005, is maintained. New Claims 47-54 are herein rejected under 35 U.S.C. 102(b) as being anticipated by Adney et al, 1994 or Tucker et al, 1989 for the same reasons.

In support of their request that said rejection be withdrawn, Applicants provide the following arguments. The rejection postulates an unwarranted assumption that the cellulases in Adney et al., 1994 or Tucker et al. 1989 are identical to AviIII of the present invention. Applicants then go on to described that, because of the differences in molecular weights, the protein of SEQ ID NO: 1 cannot be any of the cellulase of Adney et al or Tucker et al.

Applicants' argument refers to the declaration submitted August 1, 2002 which provides evidence regarding the inability of Acidothermus to glycosylate cellulases and the serendipitous discovery of AviIII, which was discovered as a xyloglucanase gene attached to an endoglucanase fragment when screening for endoglucanases.

These arguments are not found to be persuasive for the following reasons. Applicants' response is not relevant to the instant rejection. As stated in the prior action, Claims 1, 2, 4-12, 14, 28, 36, and 43, and new Claim 47-54 herein, are rejected under 35 U.S.C. 102(b) as being anticipated by Adney et al, 1994 or Tucker et al, 1989 because both of Adney et al and Tucker et al teach a "**composition comprising the culture supernatant of *Acidothermus cellulolyticus***" (Examiner's instant emphasis). A person of ordinary skill in the art would believe, it is more likely than not, that said culture supernatant contains the cellulase of SEQ ID NO: 1, which is made by *A. celluloyticus* and has a signal sequence and would, thus, be secreted from the cell. The instant rejection is not based on any assertion that the polypeptide of SEQ ID NO: 1 is the same as any of the polypeptides characterized by Adney et al and Tucker et al. Applicants appear to be reiterating their response to the rejection of original Claims 1-13, 28, 29, and 43 (filed June 3, 2002), as set forth in the First Action on the Merits (mailed August 1, 2002), which is not relevant here.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Rejection of Claims 1, 2, 4-12, 14, 15, and 28 under 35 U.S.C. 103(a) as being unpatentable over Mohagheghi et al, 1986 in view of Berghem et al, 1976 and Katz et al, 1968, for the reasons described in the First Action on the Merits of August 1, 2002, the Final Rejection of March 11, 2003, the RCE First Action on the Merits of June 16, 2004, and the RCE Final Rejection of May 18, 2005, is maintained. New Claims 47-58 are herein rejected under 35 U.S.C. 103(a) as being unpatentable over Mohagheghi et al, 1986 in view of Berghem et al, 1976 and Katz et al, 1968, for the same reasons.

In support of their request that said rejection be withdrawn, Applicants provide the following arguments.

(A) "To establish prima facie obviousness of a claimed invention, all the claim limitations must be taught or suggested by the prior art." See MPEP 2143.03. At present, no reference teaches or suggests the GH74 family polypeptide that is claimed. This is an exoglucanase or modified exoglucanase, for example, as shown in SEQ ID NO. 1. In contrast, Mohaghegi et al. 1986 in view of Berghem et al. 1976 and Katz et al. 1968 uses Berghem et al. to show the isolation of a cellulase, but the cellulase is an endoglucanase. Therefore, this cannot be the GH74 family polypeptide that is claimed. As Paragraph 9 of the Rule 132 Declaration filed December 26, 2002 makes clear, the claimed GH74 domain functions as an exoglucanase, not an endoglucanase. It follows that the combination does not teach or suggest all of the claim limitations because the combination, if proper, would merely result in the isolation of an endoglucanase from A. cellulolyticus. Therefore, Mohaghegi et al. 1986 in view of Berghem et al. 1976 and Katz et al. 1968 does not teach the isolation of an exoglucanase.

(B) Furthermore, in order to establish a prima facie case of obviousness, the references must provide sufficient guidance and enabling methodology for practicing the claimed invention with reasonable expectation of success. Examiner has acknowledged in the Office Action dated June 16, 2004 that Claim 1 of the application recites "substantially purified AviIII peptide," and that a protein preparation would not be deemed purified for the purpose of the present invention if the preparation contains more than about 10% of contaminating substances. There is no indication that Berghem et al. has achieved this level of purity. In fact, Berghem teaches the purification up to a point when the peaks for 280 nm absorbance and avicelase activity coincide (See e.g., Fig. 6). However, as is well known in the field, contaminating proteins sometimes co-purify with the target protein. Just because the peaks for 280 nm absorbance and avicelase activity coincide does not mean that Berghem has achieved a purity of more than 90%. Without a showing of purity commensurate with that of the present invention, the three references, taken as a whole, do not provide enabling methodology with reasonable expectation of success to motivate one of ordinary skill to attempt to prepare the exoglucanase of the present invention to a purity of about 90%. Applicants respectfully request withdrawal of the 35 U.S.C. 103 rejections.

(C) The Examiner on page 124 of the present office action clarifies that the Berghem reference is not cited to show purification of the claimed exoglucanse, rather, Berghem is cited to show methods that would or might be useful in purifying an exoglucanase. We fail to understand this use of Berghem because we are claiming a composition, not a method. This use of Berghem is inapposite to 35 U.S.C. 103(a), which says "[p]atentability shall not be negatived by the manner in which the invention was made". The Examiner relies upon Berghem- a reference that

used methodology resulting in the purification of an endoglucanase, not an exoglucanase. If anything, Berghem teaches away from the composition that is claimed because a purified endoglucanase should have resulted from this methodology.

These arguments are not found to be persuasive for the following reasons.

(A) Reply: This is the same argument put forth by Applicants in their remarks of December 26, 2002. Applicants are referred to the Examiner's response provided in the Final Rejection of March 11, 2003.

(B) Reply: The specification defines "'Purify' or 'purified'" as "a target protein that is free from at least 5-10% of contaminating protein" (pg 12, lines 12-13), not a protein that is free of 90% of contaminating protein. Thus, Applicants' instant argument that "a protein preparation would not be deemed purified for the purpose of the present invention if the preparation contains more than about 10% contaminating substance" is not supported by the specification.

As explained in the Final Rejection of March 11, 2004 (pg 5, parg 2), Berghem et al teach the methods of molecular sieve chromatography, dipolar adsorbent chromatography, isoelectric focusing, and affinity chromatography on an Avicel column for purification of cellulases (pg 622, parg 2-8 in Berghem et al). A person of ordinary skill in the art would believe that, more likely than not, any one of said methods would remove at least 5-10% of contaminating protein, while combining multiple said methods would result in a highly purified enzyme, even if one or a few co-purifying proteins are present.

(C) Reply: It is acknowledged that Berghem et al teaches a method, not a composition or product. However, because the instant rejection is under 35 U.S.C. 103(a), not 35 U.S.C. 102,

it is not necessary for Berghem et al to teach a composition or product. Berghem et al is merely required to provide what is lacking in Mohagheghi et al to attain the recited invention. As explained in the First Action on the Merits of August 1, 2002, Mohagheghi et al teach *A. celluloyticus* but do not teach the isolation of cellulases therefrom. Berghem et al provides what is lacking in Mohagheghi et al, i.e. methods for isolating cellulases from *A. celluloyticus*, to attain the recited invention.

Berghem et al do not teach away from the instant invention, because as explained in detail in the Final Rejection of March 11, 2003 (pg 5-6) the methods of Berghem et al can be used to isolate both exoglucanases and endoglucanases.

For these reasons and those set forth in the First Action on the Merits of August 1, 2002, the Final Rejection of March 11, 2003, the RCE First Action on the Merits of June 16, 2004, and the RCE Final Rejection of May 18, 2005, rejection of Claims 1, 2, 4-12, 14, 15, and 28 under 35 U.S.C. 103(a) as being unpatentable over Mohagheghi et al, 1986 in view of Berghem et al, 1976 and Katz et al, 1968, is maintained. New Claims 47-58 are herein rejected under 35 U.S.C. 103(a) as being unpatentable over Mohagheghi et al, 1986 in view of Berghem et al, 1976 and Katz et al, 1968, for the same reasons.

Examiner's note: It is noted that the file for the instant applicant contains 129 documents, many more than average for prosecution of an application. It is noted that Applicants' responses to the Office's actions are often fraught with errors. For example, in the instant response of September 2, 2005, Claims 47 and 50 were improperly formatted and the substitute specification was not filed. In the interest of compact prosecution, it is suggested that the Applicants carefully consider the instant action and carefully compose their response.

Applicant is again reminded that any amendment to the specification, which introduces New Matter, cannot be entered.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sheridan L. Swope whose telephone number is 571-272-0943. The examiner can normally be reached on M-F; 9:30-7 EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Kathleen Kerr can be reached on 571-272-0931. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published application may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on the access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Sheridan Lee Swope, Ph.D.

Art Unit 1656

SHERIDAN SWOPE, Ph.D.
PATENT EXAMINER